REMARKS

These remarks are in response to the final Office Action mailed May 27, 2004. Claims 53 and 54 have been added. The amendment introduces no new matter. Claims 17, 32-40, 42-46, 53, and 54 will be pending upon the entry of the amendment.

A. Rejection Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 17 and 32-39 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. The rejection is respectfully traversed.

The Examiner is required to satisfy the burden of demonstrating that the inadequate written description rejection is proper. See, *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976). A strong presumption of adequacy of written description exists and § 112, paragraph 1 rejections of an original claim should be rare. See, MPEP §§ 2163(I)(A) and 2163(II)(A). It is respectfully submitted that in this case the Examiner has not met this burden.

The description is considered adequate if "the disclosure of the application relied upon reasonably conveys to the artisan that the inventor had possession … of the … claimed subject matter [at the time of filing]." See, *Wang Labs Inc. v. Toshiba Corp.*, 993 F.2d 858, 26 USPQ2d 1767. In other words, the question of the lack of adequate written description does not arise unless "one skilled in the art [would not be able] to immediately envisage the product claimed…" *Fujikawa v. Wattanasin*, 93 F.3d 1559, 39 USPQ2d 1895. It is submitted that applying these broad principles to the present application, it can be unequivocally concluded that the written description in this application adequately supports the claims.

More particularly, the Examiner has asserted (item 15, page 5 of the Office Action) that neither the active target members nor the common functionality for conjugation of the probe to the target members are identified in the specification. The Examiner also objected to the alleged narrowness of examples which are directed, according to the Examiner, only to detection of serine hydrolases (page 7, first paragraph of the Office Action). The Applicants respectfully disagree, on the following grounds.

With respect to the "identifying characteristics" of active target members, the specification first defines (paragraph [0075]) an "active protein" as "a protein, e.g., enzyme, in its normal wild type conformation," thus indicating to those having ordinary skill in the art what a large class of active target members to be analyzed is.

Next, the specification does provide a list of a large number of these target members. The list includes many target members, not just serine hydrolases. The examples of the target members that are provided include (paragraph [0074]):

> "enzymes, included in the groups oxidoreductases, hydrolases, ligases, isomerases, transferases, and lyases and include such enzymes or enzyme groups as serine hydrolases, metallo-hydrolases, dehydrogenases, e.g. alcohol and aldehyde dehydrogenases, and nucleotide triphosphate (NT)-dependent enzymes, although, the invention envisions ABPs which recognize any protein, e.g., enzyme, family. Other proteins include proteins that bind to each other or to nucleic acids, such as transcription factors, kringle structure containing proteins, nucleic acid binding proteins, G-protein binding receptors, cAMP binding proteins, etc."

The specification also discloses other target members, e.g., such as various receptors, transcription factors, G-proteins, ion channels, protein inhibitors, etc. (page 47, paragraph [0119]).

With respect to the "common functionality" in the target members for conjugation of the probe to the target members, the specification first defines (paragraph [0104]) the "common functionality" as the "same functionality at the active size." Then, the "common functionality" is provided by giving examples of the chemical reactive groups of activity-based probes which can react with such "common functionality." These examples include (paragraph [0105]) "diazoketone, arylazide, psoralen, arylketone, arylmethylhalide, etc." It is clearly within the knowledge of those having ordinary skill in the art which "common functionalities" can react with diazoketone, arylazide, psoralen, arylketone, or arylmethylhalide reactive groups of the probe. In addition, the specification also provides a specific example of "common functionalities," e.g., "sulfhydryl groups" for which the reactive groups of the probe can be "olefins and acetylenes to which are attached electron withdrawing groups such as a sulfone, carbonyl, or nitro group." See, paragraph [0105].

Further guidance is provided in the specification with regard to with respect to the selection of the target proteins and the common functionalities present in the target proteins. The specification provides at page 46, paragraph [0118]:

> "For many of the enzyme genera, functionalities are known that do not significantly react with enzymes of other genera, particularly non-enzymatic proteins and enzymes that have different reactive sites. It is ... desirable that the functionality does not react with inactive target enzyme."

It is submitted that the above mentioned parts of the specification do describe both the active target members and their common functionalities with sufficient clarity and specificity, so as to convey to those having ordinary skill in the art that at the time of application the Applicants did have possession of the claimed invention. It is further submitted, that even if the specification listed only just a few of such active target members, it would be still sufficient. It has been established law that the "written

description requirement may be satisfied through sufficient description of a representative number of species..." *University of California v. Eli Lilly and Co.*, 119 F.3d at 1568, 43 USPQ2d at 1406 (Fed. Cir. 19970). There is no need to provide individual support for each species in the genus, and the description of a "representative number of species" is adequate. *In re Bell,* 991 F.2d 781, 785 26 USPQ2d 1529, 1532 (Fed. Cir. 1993).

The Examiner further asserted that the specification describes a specific probe (FP-biotin, FP-peg-biotin) which in the Examiner's view is not an adequate representation regarding the active target members for which this probe is intended (page 6, first paragraph of the Office Action). The Examiner is mistaken.

The Applicants direct the Examiner's attention to paragraph [0083] of the originally filed specification (pages 28-29), which provides a large number of examples of probes that can be used. The probes can include:

> "an alkylating agent, acylating agent, ketone, aldehyde, sulphonate or a phosphorylating agent. Examples ... include, but are not limited to fluorophosphonyl, fluorophosphoryl, fluorosulfonyl, alpha-haloketones or aldehydes or their ketals or acetals, respectively, alpha-haloacyls, nitriles, sulfonated alkyl or aryl thiols, iodoacetylamide group, maleimides, sulfonyl halides and esters, isocyanates, isothiocyanantes, tetrafluorophenyl esters, N-hydroxysuccinimidyl esters, acid halides, acid anhydrides, unsaturated carbonyls, alkynes, hydroxamates, alpha-halomethyl hydroxamates, aziridines, epoxides, or arsenates and their oxides. Sulfonyl groups may include sulfonates, sulfates, sulfinates, sulfamates, etc., in effect, any reactive functionality having a sulfur group bonded to two oxygen atoms. Epoxides may include aliphatic, aralkyl, cycloaliphatic and spiro epoxides, the latter exemplified by fumagillin, which is specific for metalloproteases."

Finally, the Applicants respectfully point out that particular examples of the probes provided in the specification (including examples) are merely illustrative and not intended to be limiting, and it is so stated in the specification.

In view of the foregoing, the Applicants submit that the present specification contains a complete description of the invention sufficient to demonstrate that the Applicants, at the time the application was filed, had possession of the claimed invention. Accordingly, it is respectfully submitted that the rejection of claims 17 and 32-39 under 35 U.S.C. § 112, first paragraph, as allegedly lacking adequate written description, is not properly applied. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

B. Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 36 has been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being incomplete for omitting essential steps. The rejection is respectfully traversed.

The Applicants respectfully disagree that the method is incomplete or that any essential steps have been omitted. With respect to the Examiner's suggestion that the step is needed reciting how the probes enter the cell to conjugate with the target protein, it is submitted that claim 17 recites that the process is conducted "under conditions for conjugation of said probe(s) to said target members." Those having ordinary skill in the art know what those conditions are. Some typical conditions are provided in examples, and throughout the specification (e.g., *inter alia*, in paragraph [0139] on page 55).

With respect to the Examiner's suggestion that the step is needed reciting how the conjugated probes are determined, claim 17 recites that "the presence of said adduct in said mixtures is **indicative** of the presence of active target members in said mixtures."

Those having ordinary skill in the art clearly recognize that the no additional steps are required to practice the invention, because just the presence of the adduct is sufficient to determine the presence of an active protein. Thus, the method at issue is complete as currently presented.

Accordingly, it is submitted that claim 17 is written with sufficient specificity and no further steps are need to be added. Claim 36 depends on claim 17 and includes all the steps recited in claim 17. For the reasons set forth above, it is respectfully submitted that the rejection of claim 36 under 35 U.S.C. § 112, second paragraph, do not apply. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

C. <u>Rejections Under 35 U.S.C. § 102(e) and § 102(b)</u>

Claim 17 has been rejected under 35 U.S.C. § 102(e), as allegedly being anticipated by US Patent No. 6,197,599 to Chin et al. (item 19 on page 10 of the Office Action). Claims 17, 32, and 36 have been additionally rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Purohit et al. (*Biochemistry*, 1995, 34(36):11508-11514) (item 26 on page 16 of the Office Action). These rejections are respectfully traversed.

With respect to the Chin et al. reference, Chin et al. describe using protein arrays immobilized on a substrate for detection of proteins in a sample (Abstract, Col. 5, lines 18-22). For example, arrays of antibodies affixed to glass plates or membranes are used to capture cellular proteins (Col. 5, lines 20-22).

Chin et al. fail to teach even the formation of a conjugate or adduct formed as a result of interaction between the antibodies of the array and the cellular protein. Assuming, *arguendo*, that such an adduct can be formed despite Chin et al.'s silence concerning the formation thereof, Chin et al. fail to teach that the presence of such adduct "is indicative of the presence of active target members in said mixtures, wherein said

related proteins include a common functionality for conjugation at an active site," as recited in claim 17.

With respect to Purohit et al. reference, Purohit et al. teach simple protein inhibition. For instance, the inhibition of sulfatase enzymes is described. A single compound belonging to the estrone group, illustrated by Figure 1 on page 11508, Col. 2 in the Purohit et al. reference, can be used for the inhibition. Purohit et al. teach that any of compounds (1)-(6) shown by Figure 1 of the reference (e.g., EMATE) can be used; however, using more than one of them simultaneously is not described. Accordingly, Purohit et al. fail to teach using plurality of probes. Thus, using more than one activity-based probe limitation recited in claim 17 is not taught by Purohit et al.

Therefore, while the present invention allows profiling classes of proteins in a sample on the basis of changes in protein activity rather than simply variations in protein level, what is described in Purohit et al. merely teaches protein inhibition but does not provide for differentiating a complex mixture of proteins on the basis of activity.

Accordingly, claim 17 is patentably distinguishable over both Chin et al. and over Purohit et al. Each of claims 32 and 36 depends on claim 17 and is consequently patentably allowable for at least the same reason. Reconsideration and withdrawal of the rejection of claims under 35 U.S.C. § 102(b) and § 102(e) are respectfully requested.

D. Rejection Under 35 U.S.C. § 102(a)

Claims 17, 32-36, 38, 40, 42, and 46 have been rejected under 35 U.S.C. § 102(a), as allegedly being anticipated by Liu et al. (*PNAS*, 1999, 96(26):14694-14699) (item 21 on page 12 of the Office Action). This rejection is respectfully traversed.

The Applicants respectfully renew their previous argument that Liu et al. is not available as a prior art reference either under 35 U.S.C. § 102(a) or 35 U.S.C. § 103(a)

since the subject matter set forth in Liu et al. was derived from the Applicants' own work. The Examiner rejected this argument (item 22, page 13, and item 24, page 15, of the Office Action) because the inventive entity in the present application (Cravat, Sorensen, Patricelli and Lovato) is different from the authorship of the Liu et al. reference after the removal of Mr. Liu's name (leaving Cravat and Petricelli). The Examiner's position is incorrect and does not conform to the existing law for the following reasons.

It has been for many years a well established law that a publication that is used as a ground for a § 102(a) and/or § 103(a) rejection can be effectively removed if an applicant can file a declaration under 37 C.F.R. § 1.132. The declaration must establish that the applicant is a sole inventor of the subject matter disclosed in the publication, while the other co-author of the publication was working under the declarant's direction. *In re Katz*, 687 F.2d 450, 215, 215 USPQ 14 (CCPA 1982), MPEP § 715.01(c). This situation is further discussed in MPEP § 716.10. The Applicants particularly direct the Examiner's attention to the end of MPEP § 716.10, where Example 2 describes the situation identical to the situation in this case.

Example 2 in MPEP § 716.10 analyzes a situation when a reference describing the claimed invention is found, and the author of the reference is different from the applicant. In this case, the Examiner cited a reference (Liu, Cravatt, Petricelli) that allegedly rendered claims 17, 32-36, 38-40, 42, and 46 anticipated. An Applicant (Cravatt) declared under § 1.132 that the relevant parts of the reference originated with him, and that a co-author of the reference (Liu) did not contribute to the mental conception of the present invention. Such a declaration was previously submitted to the Examiner in this case. Under MPEP § 716.10 and applicable case law, the previously submitted declaration is sufficient to remove Liu et al. as an anticipatory reference.

With regard to the Examiner's observation that the Liu et al. reference and the current application have different inventive entities, this makes no difference. A "printed

publication" reference under § 102(a) is proper if, **prior to the time of an invention**, it described subject matter that is claimed in a later filed application. Clearly, if Liu did not contribute to the claimed subject matter, this leaves only Cravatt and Petricelli. Consequently, it would be impossible to publish an article describing the claimed subject matter before it was invented.

In view of the foregoing, it is respectfully submitted that Liu et al. cannot serve as a proper reference and claim 17 is allowable over this reference. Each of claims 32-36, 38-40, 42 and 46 depends, directly or indirectly, on claim 17 and is consequently patentably allowable for at least the same reason. Reconsideration and withdrawal of the rejection of claims under 35 U.S.C. § 102(a) are respectfully requested.

E. Rejection Under 35 U.S.C. § 103(a)

Claims 17, 32-40, 42, and 46 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Liu et al. and US Patent No. 5,151,164 to Blanchard et al. (item 23 on page 13 of the Office Action). This rejection is respectfully traversed.

As discussed above, Liu et al. cannot serve as a proper reference to make claim 17 obvious. Blanchard et al. alone does not teach or suggest every limitation of claim 17. Blanchard et al. disclose capillary electrophoretic process and a device to carry this process, for example, for separating the proteins. There are no teachings or suggestions in Blanchard et al. alone providing that "related proteins include a common functionality for conjugation at an active site," as recited by claim 17.

Consequently, claim 17 is patentably distinguishable over the cited art. Claims 32-40, 42, and 46 depend on claim 17, directly or indirectly, and are patentable for at least the same reasons. Accordingly, reconsideration and withdrawal of the § 103(a) rejection of claims 17, 32-40, 42, and 46 are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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